

corresponding number of claims. The amendments do not raise the issue of new matter.

Entry of the above amendments and consideration of the following are requested.

Entry of the above amendments will, at a minimum, reduce the issues for appeal, as described below.

The Examiner is requested to hold in abeyance the obviousness-type double patenting rejection of the pending claims over the claims in co-pending Application No. 08/776,350, until such time is allowable subject matter is identified.

The Section 102 rejection claims 13-20 over Martuza (U.S. Patent No. 6,139,834), will be moot upon entry of the above amendments.

The amended claims are submitted to be patentable over Martuza such that entry of the above amendments is believed to reduce the issues for appeal by obviating at least the Section 102 rejection over the same. The Examiner's consideration of the following in this regard is requested.

The Examiner has characterized the teaching of Martuza as including "the delivery of a pharmaceutical composition comprising: (A) a herpes simplex virus vector that is altered in (i) the  $\gamma$ 34.5 gene, and (ii) the ribonucleotide reductase gene". See, page 3 of the Office Action dated December 5, 2001 (Paper No. 14). The applicants believe that Martuza teaches the modification of the ribonucleotide reductase gene as being an essential feature of their invention

and that Martuza indicates that the ribonucleotide reductase negative mutants are avirulent and, as such, the inclusion of a modified ribonucleotide reductase gene is "essential to a therapeutic vector". See, column 6, lines 40-45 of U.S. Patent No. 6,139,834. The applicants believe the paragraphs spanning lines 49-67 of column 6 of Martuza discusses mutants deficient in only the  $\gamma$ 34.5 gene as being attenuated for neurovirulence which reduces the possible damage to normal brain cells. Thus, the applicants believe that Martuza teaches away from using a mutant having a  $\gamma$ 34.5 gene mutation without a modification in the ribonucleotide reductase gene, for non-neuronal treatment.

The invention of the amended claims clearly indicates that a mutant containing a modification of the ribonucleotide reductase gene, which is an essential element of the cited art, is not included in the claimed method. Accordingly, the amended claims are submitted to be patentable over Martuza.

The Section 103 rejection of claims 13-22 over Martuza in view of MacLean (J. Gen. Virol. 72:631-639, 1991) or Brown (WO 92/13943) and Markert (Neurosurgery, 32:597-603, 1993) will be moot upon entry of the above amendments. The amended claims are submitted to be patentable over the cited combination of art as none of the secondary references teach that Martuza's mutant, which contains as an essential element a modification of the ribonucleotide reductase gene, should be altered to exclude the same. Accordingly, the cited art failed to suggest the invention of the amended claims. The claims are submitted to be patentable over the cited art.

The Section 112, second paragraph, rejection of claims 13-22 cited on page 12 of Paper No. 14 will be moot upon entry of the above amendments. The claims have been amended to provide appropriate antecedent basis, as indicated by the Examiner. The claims are therefore submitted to be definite.

Entry of the above amendments and an indication of allowance or allowable subject matter are requested. The Examiner is requested to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



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